

REMARKS/ARGUMENTS

According to the Office Action, claims 1-60 are pending in this application. In fact, the application includes Claims 1-66. As a result of the finality of the Restriction/Election requirement communicated in the Office Action mailed on October 3, 2003, Claims 1-12 and 31-66 (not 60) have been withdrawn from consideration. Claims 13-30 stand rejection under 35 U.S.C. §102. With the present amendment, Claims 1-12, and 31-66 have been canceled, Claims 13 and 27 have been amended, and new Claims 67-76 have been added. The amendments and the new claims do not add new matter. Specific support for the amendments in Claims 13 and 27 is at least at page 11, line 15. The new claims are supported throughout the specification, including the examples, the original claims, and page 2, line 15; page 18, lines 5-19; page 21, lines 13-16; and page 22 lines 8-16 of the specification.

Restriction/Election

Applicants note the finality of the restriction requirement, which is reflected in the present Office Action.

Information Disclosure Statement

Applicants note that references which are not in English language have not been considered by the Examiner in the absence of a concise explanation of their relevance. Applicants will provide a concise explanation shortly.

Claim Rejections - 35 U.S.C. §102

Claims 13-30 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by U.S. Patent Application Publication No. 2002/0028488 (3/7/02) (Singh et al.).

Singh et al. describes the generation of transgenic birds making human or chimeric antibodies. It has no teaching or suggestion to make human or chimeric antibodies in any other animal species. Claims 13 and 27 of the present application have been amended to exclude birds. Accordingly, Singh et al. does not anticipate Claims 13, 27, or any of the dependent claims, which, directly or indirectly, all claims the recitations of Claims 13 and 27. Accordingly, the rejection of Claims 13-30 should be withdrawn.

Singh et al. does not anticipate the newly added claims either. Singh et al. teaches the generation of transgenic birds expressing human or chimeric immunoglobulin by (1) disruption or inactivation of the endogenous Ig loci, and (2) insertion of an exogenous Ig locus, or a part of an exogenous Ig locus. The disruption or inactivation of the exogenous loci may or may not be performed in the same step as insertion of the exogenous locus, or an part of it. This process is schematically illustrated in Figure 4 of Singh et al. The exogenous sequences can be inserted by homologous recombination at the site of the endogenous heavy or light chain locus, in which case the transgenic vectors comprise a human Ig locus, or part of a human Ig locus, flanked by sequences homologous to genomic bird sequences. If the insertion is random, the flanking sequences are not needed.

Accordingly, in its closest disclosure, Singh et al. teaches vectors containing human immunoglobulin sequences flanked by chicken sequences. In contrast, the vectors claimed in newly added Claims 67-76 of the present application (1) retain the regulatory sequences of the exogenous Ig locus, and (2) comprise two or more human Ig coding sequences, sequences flanked/separated by non-coding sequences from the non-human recipient animal. In other words, in the vectors of claimed in Claims 67-76, non-coding sequences of the recipient non-human animal are retained, and only coding sequences are replaced by coding sequences of a human Ig polypeptide. This structural difference relative to the vectors of Singh et al. is very significant, since there is experimental evidence that in birds (*e.g.*, chicken) the insertion of a human Ig locus, without retaining the exogenous non-coding (regulatory sequences), does not support antibody diversification by gene conversion effectively. In contrast, the vectors of the present application, once introduced into non-human animals, such as birds, support expression of chimeric and human antibodies and diversification of the antibody repertoire by gene conversion.

In view of the foregoing arguments, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

All claims pending in this application are *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. 08-1641, referencing Attorney's Docket No. 39691-0005 A). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully Submitted,

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By: Daphne Reddy
Daphne Reddy (Reg. No. 53,507)

HELLER ERHMAN WHITE & McAULIFFE LLP

275 Middlefield Road
Menlo Park , California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

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